Antibiotics prescription pattern in COVID-19 patients presenting in DHQ Teaching Hospital Sahiwal; Is Pakistan heading towards Post-COVID Antibiotic Resistance Era?

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Abstract

Objective: To determine frequency and pattern of antibiotic prescription in COVID-19 patients presenting in DHQ teaching hospital, Sahiwal.

Material and Methods: This observational cross-sectional prospective study was conducted from 1st June 2020 to 31st March 2021 in patients admitted in COVID isolation facility of DHQ Teaching hospital, Sahiwal with confirmed COVID-19 infection. Patients of all ages and of both genders were included. Data was collected by a pre-designed proforma. Data included patient's age, gender, co-morbid conditions, type and duration of antibiotic use, and details of prescribing physicians. Descriptive statistics were applied to determine frequency and percentages of variables.

Results: Out of 800 participants, 543 (67.8%) were males, and the remaining 257 (32.1%) were females. Majority 328 (41%) of patients belonged to age group 40-60 years. 639 (79.8%) patients had co-morbidities. Diabetes mellitus was the most common co-morbid condition 248 (31%). Antibiotics were prescribed to all patients 800 (100%) before admission to the COVID Isolation facility. The majority of patients 348 (43.5%) had used antibiotics for 3-7 days before admission. Macrolides class was the most commonly prescribed antibiotic 417 (52.1%). General practitioners had more tendency to prescribe antibiotics 509 (64%) as compared to medical specialists 212 (26.5%) and pulmonologists 79 (9.8%).

Conclusion: Antibiotic stewardship needs to be improved in COVID-19 patients and prescription should be evidence-based aided by laboratory tests. Development of local guidelines for judicious antibiotic prescription in COVID-19 will help in preventing antibiotic resistance.

Keywords: Antibiotics, antibiotic resistance, COVID-19, drug prescription, SARS-CoV-2.

Introduction

After the very fortunate discovery of penicillin, the treatment of bacterial infections stepped into a new era. This revolution had a huge impact on the world during world war when hundreds of thousands of soldiers got relief from infected wounds and the later impact was passed on to the post-war era. With the discovery of penicillin, there was huge research in pharmacology and microbiology of microscopic organisms and their drug formulations. As a result, new antibiotics with better coverage and better efficacy were formulated and marketed.[1] Antibiotic have traveled very far since the discovery of penicillin in a small duration of time with the introduction of many new classes and generations. Today these drugs have significantly reduced postoperative complications and cured millions of patients worldwide with their magical influence.[2] The introduction of broad-spectrum antibiotics is a key step in this regard. Some of these antibiotic groups include penicillins, macrolides, fluoroquinolones, and carbapenem groups.[3]

Due to magical improvement in patient's symptoms suffering from bacterial infections, antibiotic use spread dramatically all over the world including in developing countries. Unfortunately with excessive use, the phenomenon of antibiotic resistance has become a menace now.[3,4] The causes of antibiotic resistance are multifactorial including over the counter sale in many countries, the wrong choice of antibiotics for the management of infections, use of antibiotics for less than the recommended time, use of antibiotics without culture and sensitivity, and use of antibiotics in infections caused by other microorganisms including viruses, parasites, and fungi.[5,6]

COVID-19 Pandemic spread like wildfire after first cases reported in Wuhan China. Currently, it has affected more than 223 countries of the world with drastic effects on the world economy and social lives of individuals. Unfortunately, the signs and symptoms of COVID-19 share similarities with signs and symptoms of infections caused by many other microorganisms including bacteria, parasites, and fungi.[7,8] Pakistani population are very much dependent on general practitioners(GPs) and over the counter purchase of drugs from medical stores and pharmacies. From the start of the COVID-19 pandemic, there was a huge social stigma attached to COVID-19 cases due to fear in the masses and strict isolation and burial policies of the government. Due to these factors COVID-19 has been mistakenly diagnosed as enteric fever and other bacterial diseases due to lack of knowledge of GPs and to satisfy patients psychologically. As a result of these factors, a significant number of COVID-19 cases have already received antibiotics for COVID treatment upon their arrival in tertiary care hospitals. Similarly, there was a substantial non-evidence-based prescription of various drugs during COVID-19 including Hydroxychloroquine, Azithromycin, and Vibramycin to COVID cases worldwide including Pakistan.[9] Many antibiotics were "tried" on COVID cases and led to the danger of emerging antibiotic resistance.

Due to the increasing number of COVID-19 cases the use of oral or intravenous antibiotics was more and more evident. This study was planned to encompass the brutal use of antibiotics and to predict possible future antibiotic resistance which treating physicians may encounter in the management of various endemic bacterial diseases like enteric fever and UTI in a post-COVID era in Pakistan. This study is aimed to create awareness about the meticulous use of precious antibiotics to minimize post-COVID antibiotic resistance.

Materials and Methods

This observational cross-sectional prospective study was conducted in patients admitted to DHQ Teaching hospital Sahiwal with COVID-19 infection from 1st June 2020 to 31st March 2021. The study was approved by the Institutional review board of Sahiwal Medical College, Sahiwal via letter no 62/DME/SLMC/SWL.

Data was collected from 800 symptomatic patients of COVID-19 confirmed by nasopharyngeal swab PCR presenting to COVID isolation facility during the period of 1st June 2020 to 31st March 2020. Study subjects were included by convenient non-probability sampling. COVID-19 cases of all severity classes and any age and gender having suggestive symptoms (Fever, cough, body aches, shortness of breath, diarrhea) with positive PCR report of Nasopharyngeal swab for SARS-Cov-2 PCR were included. All patients who had negative PCR with or without symptoms were excluded. Data was collected on a predesigned proforma after taking informed consent. Data included demographic details, co-morbid conditions, smoking status, type and duration of antibiotic use, route of antibiotic administration, and details of prescribing physicians. Data analysis was done by using SPSS 24. Data were arranged in terms of gender, age groups, and admission status. The frequency of use of antibiotics along with the frequency of use of various

drug groups, route of administration, and prescribing doctor status was calculated using frequency tables. Descriptive statistics were applied to determine the frequency and percentages of variables.

Results

Antibiotics were prescribed and used by all 800 (100%) confirmed cases of COVID-19. The majority of the patients were males 543(67.8%) while 257 were females (32.1%). Most patients 328(41%) belonged to the 40-60 years age group followed by the above 60 age group 243(30.3%), 20-40 years age group 217(27.1%), and below 20 years 12(1.5%). (Figure 1)
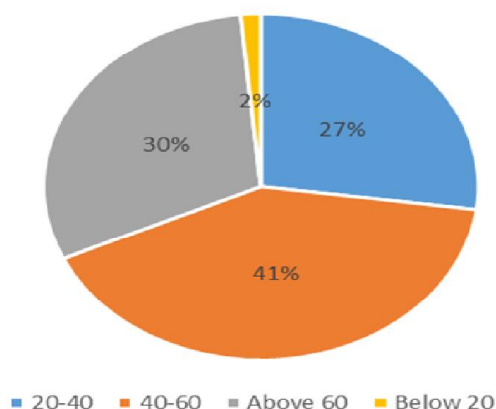
Figure 1: Frequency distribution of age groups

In the majority of cases, 509(63.6%) antibiotics were prescribed by General practitioners followed by medical specialists 212(26.5%) and pulmonologists 79(9.8%). (Figure 2)
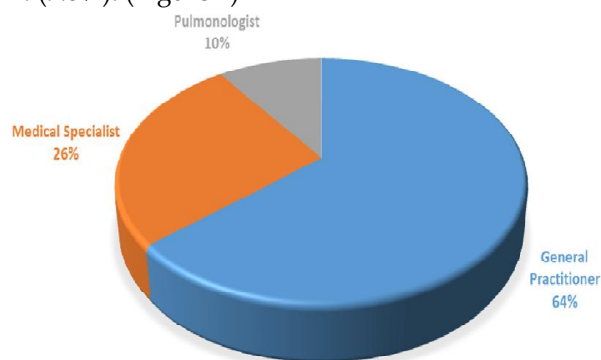
Figure 2: Frequency distribution of prescribing doctors

Comorbid conditions were present in 639(79.8%) patients. 128(20%) patients had more than one comorbidity. Diabetes was the most common co-morbidity followed by hypertension. (Table 1)

Table 1: Frequency Distribution of Comorbidities. (N=800)

Characteristics	n (%)
Smokers	118 (14.7)
Co-Morbidities	639 (79.8)
Diabetes	248 (31.0)
Hypertension	157 (19.6)
Ischemic Heart Disease	87 (10.8)
Chronic Kidney Disease	19 (2.0)
More than one Co-Morbid	128 (16.0)

As far as the route of drug administration was concerned 358(44.7%) patients used oral antibiotics while 293(36.6%) used intravenous antibiotics. 149(18.6%) patients received both oral and intravenous antibiotics. Macrolides were the most commonly prescribed group of antibiotics 417(52.1%) followed by cephalosporins 118(14.7%), Fluoroquinolones 78(9.7%), Carbapenems 59(7.3%), and tetracyclines 26(3.2%). (Table 2)

Table 2: Antibiotic Prescription pattern (N=800)

Variable	Characteristics	n(%)
Status of antibiotic use	Yes	800(100)
	No	0(0)
Route of administration	Both Oral and IV	149(18.6)
	IV	293(36.6)
	Oral	358(44.7)
Antibiotic group	Carbapenem	59(7.3)
	Cephalosporins	118(14.7)
	Fluoroquinolones	78(9.7)
	Macrolides	417(52.1)
	Tetracyclines	26(3.2)
	More than one Antibiotics	102(12.7)
Duration of antibiotic use at presentation	Less than 3 days	172(21.5)
	3 to 7 days	348(43.5)
	More than 7 days	280(35)

Discussion

Pakistan is a developing country and it has a high practice of inappropriate antibiotic use. The main factors behind this are lack of education, lack of awareness, high consultation fees of consultants, and over-the-counter sale of antibiotics.[8,10] These all factors led to inappropriate use of antibiotics in the COVID-19 pandemic as well. There has been an increase in community use of antibiotics during COVID-19.[9] The role of antibiotics in the management of COVID-19 is not proven, although antibiotics may be used later in

the course of disease in case of secondary bacterial infection. The use of inappropriate antibiotics may result in the emergence of antibiotic resistance and it has no impact on patient mortality.[11] Lack of proper antibiotic stewardship and irrational use of these useful antibiotics may lose their impact due to the ever-increasing challenge of drug-resistant enteric fever, urinary tract infection, and drug-resistant tuberculosis.[12] There should be proper stewardship of antibiotics in the management of COVID-19 cases and bacterial secondary infection should be detected by use of clinical and laboratory parameters including increased levels of serum pro-calcitonin and a second increase in CRP Quantitative levels after getting normal during disease treatment.[12]

Our study showed 100% prescription of antibiotics in the initial stage of COVID-19 infection which is per earlier studies showing brutal use of empiric antibiotics from 71-100% in COVID-19 patients.[9,13-17] There is a common practice of using antibiotics for the management of viral respiratory tract diseases due to overlapping symptoms between bacterial and viral respiratory tract infections especially by general practitioners in previous studies.[9,14] This fact is shown in our study where a high percentage of patients received antibiotics from general practitioners (63.6%). Patients were prescribed oral and intravenous antibiotics which is a common practice in Pakistan due to the over-the-counter availability of antibiotics.[18] Due to the availability of over-the-counter antibiotics in Pakistan and many other developing countries, there is a risk of anti-microbial resistance in the world.[19] Many developed countries have banned the use of antibiotics over the counter. Unlike many other studies which showed increased use of quinolones and carbapenems in COVID-19 treatment we found Macrolides to be the most common group of antibiotics used followed by cephalosporins and carbapenems.[16,20] Many antibiotics used for the management of COVID-19 have a role in enteric fever management. Extensive irrational use of macrolides group of antibiotics is alarming as it has a vital role in the management of enteric fever and its irrational use can worsen already increasing drug-resistant enteric fever in Pakistan.[21] According to WHO Pakistan is a country with a risk of extensive drug-resistant enteric fever and many developed countries have been issued travel precautions for travel in Pakistan. Another group of antibiotics fluoroquinolones has also been prescribed according to our study. Pakistan has a high percentage of Fluoroquinolone resistance. Fluoroquinolones have a major role in the management of community-acquired pneumonia and tuberculosis. The new WHO guidelines for the management of multidrug-resistant TB have the pivotal role of fluoroquinolones in them and the use of these groups of antibiotics can lead to extensive fluoroquinolone resistance which can lead to difficulty in the management of multidrug-resistant tuberculosis.[22] Similarly, macrolide and fluoroquinolone resistance is already documented in H-pylori isolates in Pakistan and any further irrational prescription can lead to an increase in resistance to H-pylori.[23] Another disease with threats of the emergence of resistance in antibiotics during its management is urinary tract infection. COVID antibiotics' inappropriate use can worsen this situation as well.[24] Use of antibiotics have also caused more cost to COVID management while trials show very cost-effective drugs for management of COVID-19 with the primary drug of treatment dexamethasone.[25]

Limitations

Due to limitations of resources, samples for antimicrobial culture and sensitivity could not be collected to assess the need for antibiotics and the resistance pattern of antibiotics. Similarly, there was no Pro-calcitonin level at the time of data collection.

Conclusion

Poor antibiotic stewardship can lead to aggravation of antibiotic resistance in a developing country like Pakistan. Post-COVID Pakistan may witness a tsunami of antibiotic resistance especially for antibiotics used in the management of enteric fever, MDR TB, H-pylori eradication, and UTI. This may lead to catastrophe in the management of the above-mentioned diseases. It is recommended to follow the antibiotic stewardship program and the use of antibiotics in COVID-19 must be decided after evaluating the patient's clinical scenario and results of biochemical tests like serum Pro-calcitonin and CRP Quantitative to avoid antibiotic resistance. The development of local guidelines for judicious antibiotic prescription in COVID-19 will help in preventing antibiotic resistance.

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